FORM PTO-1390 (Modified) (REV 10-95) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

ATTORNEY'S DOCKET NUMBER	
198323US0PCT	
U.S. APPLICATION NO. (IF KNOWN, SEE 37 CFR	
09/647924	
INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE
PCT/JP98/01712	15 April 1998
PRIORITY DATE CLAIMED	
NONE	

TITLE OF INVENTION

METHOD FOR DETECTING A GENE OF A DRUG-TARGETED PROTEIN IN A LIVING ORGANISM

APPLICANT(S) FOR DO/EO/US

Hiroyoshi HIDAKA, et al.

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☒ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. ☒ This is an express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).
4. ☒ A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.
5. ☒ A copy of the International Application as filed (35 U.S.C. 371 (c) (2))
   a. ☐ is transmitted herewith (required only if not transmitted by the International Bureau).
   b. ☒ has been transmitted by the International Bureau.
   c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US).
6. ☒ A translation of the International Application into English (35 U.S.C. 371(c)(2)).
7. ☐ A copy of the International Search Report (PCT/ISA/210).
8. ☒ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371 (c)(3))
   a. ☐ are transmitted herewith (required only if not transmitted by the International Bureau).
   b. ☐ have been transmitted by the International Bureau.
   c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
   d. ☒ have not been made and will not be made.
9. ☐ A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
10. ☐ An oath or declaration of the inventor(s) (35 U.S.C. 371 (c)(4)).
11. ☐ A copy of the International Preliminary Examination Report (PCT/IPEA/409).
12. ☐ A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371 (c)(5)).

Items 13 to 18 below concern document(s) or information included:

13. ☐ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
14. ☐ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
15. ☐ A **FIRST** preliminary amendment.
    A **SECOND** or **SUBSEQUENT** preliminary amendment.
16. ☐ A substitute specification.
17. ☐ A change of power of attorney and/or address letter.
18. ☐ Certificate of Mailing by Express Mail
19. ☒ Other items or information:

Request for Consideration of Documents Cited in International Search Report
PCT/IB/308
Letter Regarding Small Entity Status

U.S. APPLICATION NO. (IF KNOWN, SEE 37 CFR)	INTERNATIONAL APPLICATION NO.	ATTORNEY'S DOCKET NUMBER
09/647924	PCT/JP98/01712	198323US0PCT

20. The following fees are submitted:.

BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5)) :		CALCULATIONS PTO USE ONLY
☒ Search Report has been prepared by the EPO or JPO	$860.00	
☐ International preliminary examination fee paid to USPTO (37 CFR 1.482)	$690.00	
☐ No international preliminary examination fee paid to USPTO (37 CFR 1.482) but international search fee paid to USPTO (37 CFR 1.445(a)(2))	$710.00	
☐ Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2) paid to USPTO	$1000.00	
☐ International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(2)-(4)	$100.00	

ENTER APPROPRIATE BASIC FEE AMOUNT =					$860.00	
Surcharge of **$130.00** for furnishing the oath or declaration later than ☐ 20 ☒ 30 months from the earliest claimed priority date (37 CFR 1.492 (e)).					$130.00	
CLAIMS	NUMBER FILED		NUMBER EXTRA	RATE		
Total claims	5	- 20 =	0	x $18.00	$0.00	
Independent claims	1	- 3 =	0	x $80.00	$0.00	
Multiple Dependent Claims **(check if applicable).**				☒	$270.00	
TOTAL OF ABOVE CALCULATIONS				=	$1,260.00	
Reduction of 1/2 for filing by small entity, if applicable. Verified Small Entity Statement must also be filed (Note 37 CFR 1.9, 1.27, 1.28) **(check if applicable).**				☒	$630.00	
SUBTOTAL				=	$630.00	
Processing fee of **$130.00** for furnishing the English translation later than ☐ 20 ☐ 30 months from the earliest claimed priority date (37 CFR 1.492 (f)).				+	**$0.00**	
TOTAL NATIONAL FEE				=	$630.00	
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31) **(check if applicable).**				☐	**$0.00**	
TOTAL FEES ENCLOSED				=	$630.00	
					Amount to be: refunded	$
					charged	$

☒ A check in the amount of $630.00 to cover the above fees is enclosed.

☐ Please charge my Deposit Account No. in the amount of to cover the above fees.
A duplicate copy of this sheet is enclosed.

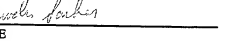
☒ The Commissioner is hereby authorized to charge any fees which may be required, or credit any overpayment to Deposit Account No. **15-0030** A duplicate copy of this sheet is enclosed.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:

22850

Surinder Sachar
Registration No. 34,423



SIGNATURE

Norman F. Oblon

NAME

24,618

REGISTRATION NUMBER

Oct 16 2000

DATE

IN THE UNITED STATES PATENT & TRADEMARK OFFICE

IN RE APPLICATION OF:

Hiroyoshi HIDAKA, et al. :

SERIAL NO: NEW U.S. PCT APPLICATION :
(Based on PCT/JP98/01712)

FILED: HEREWITH :

FOR: METHOD FOR DETECTING A GENE :
OF A DRUG-TARGETED PROTEIN IN A
LIVING ORGANISM

LETTER REGARDING CLAIM TO SMALL ENTITY STATUS

ASSISTANT COMMISSIONER FOR PATENTS
WASHINGTON, D.C. 20231

SIR:

Applicant(s) hereby give notice that Small Entity Status is claimed in the above-identified application.

Our check in the amount of $630.00 is attached hereto. If any variance exists between the amount enclosed, please charge or credit the difference to our Deposit Account No. 15-0030. A duplicate copy of this sheet is enclosed.

Respectfully submitted,
OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.

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DESCRIPTION

METHOD FOR DETECTING A GENE OF A DRUG-TARGETED PROTEIN IN A LIVING ORGANISM

Field of the Invention

The present invention relates to a method for directly detecting a gene of a target protein to which a drug is bound in a living organism following administration of the drug to the living organism.

Background Art

When a drug is proven to be effective for a certain disease, pharmacologists want to know, among other things, the action mechanism of the drug, i.e., which type of molecules (protein, nucleic acid, lipid, etc.) in cells the drug is bound to; how the drug alters the function of the molecules; and how the change in function relates to the efficacy of the drug. Until now, in general, intracellular target molecules, *inter alia*, target proteins of a drug have been determined through direct isolation of the molecules from the cells and tissue by use of a column to which the drug has been attached.

However, in the above method, the isolated proteins must be further purified for conversion into a single molecular species, and must be subjected to further amino acid sequence analysis. In order to determine the amino acid

sequence, a protein is required typically in an amount of approximately 100 μg. Thus, a large number of cells and tissue must be employed as a starting material. Even after the amino acid sequence is determined without difficulties, isolation of the gene of the molecule and determination of the nucleotide sequence are onerous and time-consuming.

Thus, an object of the present invention is to provide a method for directly detecting a gene of a target protein to which a drug is bound in a living organism after the drug is administered to the living organism.

Disclosure of the Invention

In view of the foregoing, the present inventors have conducted thorough studies, and have found that a gene of a drug-targeted protein can be directly detected by causing an antigenic substance such as serum albumin to be bound to the drug via a chemical cross-linker; using the obtained material as a probe in screening the gene by use of a cDNA expression library containing a variety of genes of a drug-administered organism, e.g., a human. The present invention has been accomplished on the basis of this finding.

Accordingly, the present invention provides a method for detecting a gene of a drug-targeted protein in a living organism, which method comprises causing an antigenic substance to be bound to a drug via a chemical cross-linker, the drug being used for administration to the living organism; using the obtained material as a probe; and

directly screening the gene of the protein bound to the probe by use of a cDNA expression library containing genes of the living organism to which the drug is to be administered.

Best Modes for Carrying Out the Invention

The method of the present invention for detecting a gene is directed to a method for directly detecting a gene of a target protein to which a drug is bound in a living organism following administration of the drug to the living organism. The drug is administered to a living organism, preferably to mammals, particularly preferably to the human body. The drug is preferably a non-protein substance which *per se* exhibits no antigenicity, in other words, is not immunogenic. Needless to say, a drug which exhibits no protein-binding capacity after being absorbed into the living organism cannot be employed in the present invention.

In the present invention, a substance in which an antigenic substance is bound to the drug via a chemical cross-linker is employed as a probe. No particular limitation is imposed on the chemical cross-linkers so long as they provide a group which cross-links a functional group of the drug and a functional group of the antigenic substance. Examples include glutaraldehyde, hexamethylene diisocyanate, hexamethylene diisothiocyanate, N,N'-poly(methylene)bis(iodoacetamide), N,N'-ethylenebis(maleimide), ethylene glycol bis(succinimidyl) succinate, sulfosuccinimidyl-4-(p-maleimidophenyl) butyrate,

and bisdiazobenzidine. When a drug has no group which can react with such cross-linkers, an appropriate functional group must be chemically introduced into the drug. In this case, the action of the drug, such as physiological action, must not be lost. Thus, the drug is preferably a substance having a functional group which is able to react with such cross-linkers.

Preferably, the antigenic substance is a substance which *per se* has immunogenicity because the antigen-antibody reaction is advantageously employed to screen a gene which is bound to a probe. In addition, preferably, the target antibody of the antigenic substance is easily available, and the antigenic substance has a low binding property to other biocomponents. For these reasons, antigenic substances such as serum albumin and fluorescein isothiocyanate (FITC) are preferred, with bovine serum albumin (BSA) being particularly preferred. The antibody against BSA is easily available, and BSA is a predominant protein component in the blood. In addition, BSA does not readily form bonds to other biocomponents, thereby exhibiting no non-specific background during screening. Therefore, BSA is a particularly preferred antigenic substance.

The conditions of the cross-linking reaction between a drug and an antigenic substance vary in accordance with the cross-linker employed. For example, a cross-linking reaction may be carried out in a solvent at room temperature with stirring.

The cDNA expression library which is employed in the present invention preferably contains a variety of genes of mammals, particularly human genes, and examples include a human brain-originating cDNA library and a human placenta-originating cDNA library. Examples of such cDNA libraries include cDNA libraries of a vector such as plasmid or phage, with cDNA libraries containing phage as a vector being preferred and cDNA libraries containing λ phage as a vector being particularly preferred. Furthermore, cDNA libraries containing λ phage (*E. coli* as a host) as a vector are particularly preferred in view of ease of cloning. Examples of such commercially available cDNA libraries include human placenta/λTrip1 Ex library.

Screening of a target gene from the aforementioned cDNA libraries is carried out, for example, in the following manner. Specifically, a DNA library and host cells are seeded onto an agar medium, where viruses are proliferated to a certain concentration, making them produce protein. The produced protein is adsorbed and fixed on a nitrocellulose membrane. The membrane is reacted with the aforementioned probe, and plaques of probe-bound phages are detected through a chemical luminescence method employing an anti-antigenic-substance antibody (e.g., anti-BSA antibody) labeled with an enzyme such as HRP (horse radish peroxidase), serving as a secondary antibody. DNA is recovered from the thus-identified plaques, and the gene of the target protein incorporated into the DNA is analyzed using a routine method.

In another possible approach, a drug is directly labeled with an enzyme such as HRP employing a chemical cross-linker without using a secondary antibody. In this case, the enzyme activity must not be lowered due to chemical reaction.

When the gene of a drug-targeted protein is successfully analyzed, the target protein is readily identified from the deduced amino acid sequence.

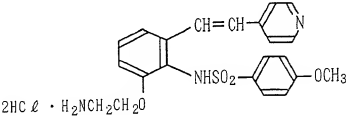
Examples

The present invention will next be described in detail by way of Examples, which should not be construed as limiting the invention thereto.

Example 1

(1) Preparation of molecular probe

As the drug, a drug (A), which is known to have excellent anti-cancer effects, represented by the following formula, was employed.



As the chemical cross linker, Sulfosuccinimidyl-4-(p-maleimidophenyl)butylate (Sulfo-SMPB) was employed. BSA was used as an antigenic substance. The compound (A) (22 mg) and Sulfo-SMPB (10 mg) were dissolved in a phosphate buffer (pH 7-9) and the resultant solution was stirred for one hour at

room temperature. Subsequently, BSA (327 mg) was added thereto and the mixture was stirred at room temperature. After completion of the reaction, the mixture was desalted using a Kwik Sep™ column, to thereby yield a probe (approximately 300 mg).

(2) Screening

A human placenta/λTrpl EX library (product of Clonetech) was employed as the cDNA library.

Firstly, in a preliminary experiment, a phage titer was determined so that about 20,000 phage plaques emerge. The phages were adsorbed onto the surface of *E. coli*, mixed with soft agar, and plated on LB agar plates (diameter: 145 mm). The number of prepared plates was 8-10. After four hours incubation at 42°C, at which point the plaques had grown to about 3-5 mm, a nitrocellulose membrane (Hybond-C Pure, diameter: 132 mm, product of Amersham) was placed carefully on the plate. Prior to placement, the membrane had been immersed in a 10 mM isopropyl-β-D-thiogalactoside (IPTG) solution for 30 minutes. In this state, the plates were incubated for an additional four hours at 37°C, to thereby produce proteins and to simultaneously cause the proteins to be adsorbed onto the membrane. Subsequently, the membranes were removed from the plates, washed with a TBST solution (the composition of which is described hereinbelow) (× 3), and subjected to blocking with a 1% gelatin solution for a period of 30 minutes to one hour. This procedure was carried out in order to suppress non-specific adsorption of

antibodies onto the membranes which were to be used later. The membranes were washed with a TBST solution (× 2) and those membranes with proteins remaining attached were immersed in a TBST solution containing probes in an amount of 1/1000 at a volume ratio. In practice, the membranes and a minimum volume of the reaction mixture (1 ml or less per membrane) are put into a plastic bag together and the bag is sealed. The bag is shaken at 4°C for 12 hours or more or at room temperature for two hours or more in order to induce the proteins to react with the probes. After the reaction, the membranes are washed with a TBST solution. Subsequently, the membranes are shaken for two hours or more in a TBST solution containing a secondary antibody (HRP-labeled BSA antibody, product of Capell, anti-BSA-rabbit-antibody-peroxidase-bound IgG fraction) in an amount by volume of 1/2,500 in order to cause the proteins to react with the secondary antibody in a way similar to that when the proteins were caused to react with the probes. After washing is performed using a TBST solution, phage plaques bound to the probes were detected using a chemiluminescence ECL system (product of Amersham). The above-mentioned procedure represents the first screening. At this stage, it is impossible to recover a single plaque. Therefore, a small region of the agar medium is cut out of the plate so that each region contains plaques having emission signals (positive clones). The agar medium was immersed in an SM solution (the composition of which will be described hereinbelow) and shaken at 4°C for 12 hours or more.

Subsequently, phages were recovered from the solution. The second screening was carried out using these phages. Phages having a titer that causes tens to a hundred plaques to emerge on an LB agar medium having a diameter of 85 mm were absorbed onto *E. coli*, and the phases mixed with soft agar were plated. The procedure of the second screening hereafter is the same as the first screening except for the addition of the competitor, drug A (10 μM) which was not bound to BSA, to the reaction mixture when reacting with probes. If this binding is dependant on the drug, the binding of the BSA-bound drug to the target plaque is inhibited by non-BSA-bound drugs which are added to the reaction mixture, and therefore, signals would be attenuated. The drug-specific binding was thus confirmed and a single positive clone was isolated. Hereafter, in accordance with the manual, the gene of the protein was recovered and the nucleotide sequence was determined.

HRP-labeled BSA antibody, the secondary antibody employed above was used after being subjected to absorption by Immobilized E. coli BNN97 Lysate (product of 5 Prime 3 Prime) in order to remove components of non-specific binding to virus-derived proteins. Each of the reagents used above has the following composition.

(a) TBST solution

10 mM Tris-HCl (pH 8.0)

150 mM NaCl

0.05% Tween-20

(b) SM solution

100 mM NaCl

10 mM $MgSO_4$

35 mM Tris · Cl (pH 7.5)

0.01% Gelatin

As a result, the target proteins to which the drug (A) is bound in living organisms were found to be thymosin β-10, NF-yB, growth hormone, and glucocorticoid hormone. Among these, NF-yB is a nuclear transcription factor and thought to be difficult to isolate by the use of the customary drug column method. Therefore, where the intracellular content is low, detection can be successfully achieved using the method of the present invention.

Industrial Applicability

The method of the present invention has eliminated the need for the protein purification step and amino acid sequence analysis, which are necessary when a conventional drug-fixed column method is performed. Also, the method of the present invention has enabled direct and simple isolation of the gene of the protein to which the drug is targeted. The invention has also enabled identification of cellular factors such as transcription factors in the nucleus, which had conventionally been difficult to purify due to the small level of such factors present in the cells.

CLAIMS

1. A method for detecting a gene of a drug-targeted protein in a living organism, which method comprises causing an antigenic substance to be bound to a drug via a chemical cross-linker, the drug being administered to the living organism; using the obtained material as a probe; and directly screening the gene of the protein bound to the probe by use of a cDNA expression library containing genes of the living organism to which the drug is to be administered.

2. A detection method according to claim 1, wherein the antigenic substance is serum albumin or fluorescein isothiocyanate.

3. A detection method according to claim 1 or 2, wherein the cDNA expression library contains a phage as a vector.

4. A detection method according to any one of claims 1 through 3, wherein the drug is non-protein and *per se* exhibits no antigenicity.

ABSTRACT

A method for detecting a gene of a drug-targeted protein in a living organism, which method includes causing an antigenic substance to be bound to a drug via a chemical cross-linker, the drug being administered to the living organism; using the obtained material as a probe; and directly screening the gene of the protein bound to the probe by use of a cDNA expression library containing genes of the living organism to which the drug is to be administered.

The method of the present invention has eliminated the need for the protein purification step and amino acid sequence analysis, which are necessary when a conventional drug-fixed column method is performed. Also, the method of the present invention has enabled direct and simple isolation of the gene of the protein to which the drug is targeted.

Declaration and Power of Attorney For Patent Application

特許出願宣言書及び委任状

Japanese Language Declaration

日本語宣言書

下記の氏名の発明者として、私は以下の通り宣言します。

As a below named inventor, I hereby declare that:

私の住所、私書箱、国籍は下記の私の氏名の後に記載された通りです。

My residence, post office address and citizenship are as stated next to my name.

下記の名称の発明に関して請求範囲に記載され、特許出願している発明内容について、私が最初かつ唯一の発明者（下記の氏名が一つの場合）もしくは最初かつ共同発明者（下記の名称が複数の場合）であると信じています。

薬物の生体内における標的蛋白の遺伝子の検出方法

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled.

METHOD FOR DETECTING A GENE OF A DRUG-TARGETED PROTEIN IN A LIVING ORGANISM

上記発明の明細書は、

- ☐ 本書に添付されています。
- ☒ 4月15日1998に提出され、米国出願番号または特許協定条約国際出願番号を PCT/JP98/01712 とし、
  （該当する場合）＿＿＿＿＿＿に訂正されました。

the specification of which

- ☐ is attached hereto.
- ☒ was filed on April 15, 1998 as United States Application Number or PCT International Application Number PCT/JP98/01712 and was amended on ＿＿＿＿＿＿ (if applicable).

私は、特許請求範囲を含む上記訂正後の明細書を検討し、内容を理解していることをここに表明します。

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

私は、連邦規則法典第37編第1条56項に定義されるとおり、特許資格の有無について重要な情報を開示する義務があることを認めます。

I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, Section 1.56.

Japanese Language Declaration
(日本語宣言書)

私は、米国法典第35編119条（a）-（d）項又は365条（b）項に基づき下記の、米国以外の国の少なくとも一ヵ国を指定している特許協力条約365（a）項に基づく国際出願、又は外国での特許出願もしくは発明者証の出願についての外国優先権をここに主張するとともに、優先権を主張している、本出願の前に出願された特許または発明者証の外国出願を以下に、枠内をマークすることで、示しています。

I hereby claim foreign priority under Title 35, United States Code, Section 119 (a)-(d) or 365(b) of any foreign application(s) for patent or inventor's certificate, or Section 365(a) of any PCT International application which designated at least one country other than the United States, listed below and have also identified below, by checking the box, any foreign application for patent or inventor's certificate, or PCT International application having a filing date before that of the application on which priority is claimed.

Prior Foreign Application(s)
外国での先行出願

Priority Claimed
優先権主張

(Number) (番号)	(Country) (国名)	(Day/Month/Year Filed) (出願年月日)	☐ Yes はい	☐ No いいえ
(Number) (番号)	(Country) (国名)	(Day/Month/Year Filed) (出願年月日)	☐ Yes はい	☐ No いいえ

私は、第35編米国法典119条（e）項に基づいて下記の米国特許出願規定に記載された権利をここに主張いたします。

I hereby claim the benefit under Title 35, United States Code, Section 119(e) of any United States provisional application(s) listed below.

(Application No.) (出願番号)	(Filing Date) (出願日)

私は、下記の米国法典第35編120条に基づいて下記の米国特許出願に記載された権利、又は米国を指定している特許協力条約365条（c）に基づく権利をここに主張します。また、本出願の各請求範囲の内容が米国法典第35編112条第1項又は特許協力条約で規定された方法で先行する米国特許出願に開示されていない限り、その先行米国出願書提出日以降で本出願書の日本国内または特許協力条約国際提出日までの期間中に入手された、連邦規則法典第37編1条56項で定義された特許資格の有無に関する重要な情報について開示義務があることを認識しています。

(Application No.) (出願番号)	(Filing Date) (出願日)

I hereby claim the benefit under Title 35, United States Code, Section 120 of any United States application(s), or Section 365(c) of any PCT International application designating the United States, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT International application in the manner provided by the first paragraph of Title 35, United States Code Section 112, I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, Section 1.56 which became available between the filing date of the prior application and the national or PCT International filing date of application.

(Application No.) (出願番号)	(Filing Date) (出願日)	(Status: Patented, Pending, Abandoned) (現況：特許許可済、係属中、放棄済)
(Application No.) (出願番号)	(Filing Date) (出願日)	(Status: Patented, Pending, Abandoned) (現況：特許許可済、係属中、放棄済)

私は、私自信の知識に基づいて本宣言書中で私が行なう表明が真実であり、かつ私の入手した情報と私の信じるところに基づく表明が全て真実であると信じていること、さらに故意になされた虚偽の表明及びそれと同等の行為は米国法典第18編第1001条に基づき、罰金または拘禁、もしくはその両方により処罰されること、そしてそのような故意による虚偽の声明を行なえば、出願した、又は既に許可された特許の有効性が失われることを認識し、よってここに上記のごとく宣誓を致します。

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Japanese Language Declaration
(日本語宣言書)

委任状：私は下記の発明者として、本出願に関する一切の手続きを米特許商標局に対して遂行する弁理士または代理人として、下記の者を指名いたします。
(弁護士、または代理人の指名及び登録番号を明記のこと)

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